

**REMARKS**

This application contains claims 1-188, the status of which is as follows:

(a) Claims 48, 178-179, and 182-184 are currently amended.

(b) Claims 2-5, 7-9, 15-18, 20-22, 25-26, 28-29, 32, 35-39, 41-46, and 49-177 have been canceled.

(c) Claims 1, 6, 10-14, 19, 23-24, 27, 30-31, 33-34, and 40 were previously withdrawn in response to the restriction requirement.

(d) Claims 185-188 are new.

No new matter has been added.

***Claim rejections under 35 U.S.C. 102 and 103***

Claims 178-184 were rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,792,100 to Shantha et al. Claims 47-48 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shantha in view of Suzuki.

***Claim 178***

While not necessarily agreeing with the rejection of independent claim 178, Applicant has amended the claim to recite that the electrical signal is applied directly to the SPG, and to remove the option of applying the electrical signal only to "nerve fibers of the subject which are directly anatomically connected to the SPG." Applicant respectfully submits that, to the extent that Shantha teaches stimulation of the SPG at all, such stimulation would be only indirect, such as via "the posterior ethmoidal nerve and orbital branch of the sphenopalatine ganglion" (col. 4, lines 50-52 of Shantha). As is well known in the art, the posterior ethmoidal nerve and the orbital branch of the SPG are nerve fibers that are anatomically connected to the SPG, and are not portions of the SPG itself. For example, this anatomy is explained in co-assigned U.S. Provisional Application 60/426,180, which is incorporated by reference in the present application (on p. 94, lines 6-7). The provisional application explains that "the retro-orbital branches of the SPG . . . are fibers that connect the SPG with orbital neural structures" (p. 9, lines 9-11 of the provisional application). Applicant thus submits that claim 178, as amended, is not anticipated by Shantha.

Furthermore, Applicant respectfully submits that claim 178, as amended, is not obvious in view of Shantha, alone or in combination with known direct SPG stimulation techniques. Any indirect activation of the SPG by Shantha's device is entirely incidental to the operation of the device as understood by Shantha. One of ordinary skill in the art would not think to combine Shantha's sphenoid sinus stimulations techniques with known direct SPG stimulation techniques. The primary motivation of Shantha's electrical stimulation of the sphenoid sinus is to treat pain by indirectly stimulating the pituitary gland: "Electrical stimulators can be placed along the outer surface of the inflatable balloon for stimulating the pituitary gland and other nerve structures surrounding the sphenoid sinus" (col. 3, lines 16-19). In the Background of the Invention, Shantha describes experimental evidence and theories supporting the efficacy of stimulation of the pituitary gland for pain relief (col. 1, line 35 – col. 2, line 24), including:

The pituitary gland is surrounded by and connected to the hypothalamus, thalamus, central gray, reticular system, hippocampus, parahippocampal cingulate gyrus. The basal ganglion, red nucleus and substantia nigra are in close proximity to the hypothalamus and are inter-linked. Electrical impulses imparted to the pituitary gland may spread to the above brain structures, and play an important role in alleviating pain and other diseases. The pituitary gland rests immediately above the thin sphenoid bone which will allow the electrical impulses to be transmitted to the surrounding, above-described brain structures. (col. 2, lines 14-24)

As is clear from this description, Shantha's understanding of the mechanism by which his device is effective does not include activation of the SPG. It would not be obvious to one of ordinary skill in the art, having read Shantha, to directly stimulate the SPG for treating pain or any of the other conditions listed in Shantha, including Alzheimer's disease.

Furthermore, Shantha provides only two brief, highly general explanations regarding why his device might treat Alzheimer's disease:

- "This device may have application in the treatment of many other diseases such as epileptic attacks, chronic fatigue syndrome, senility with hypopituitary and hyperpituitary function, dental pain, various kinds of headaches, Parkinson's disease, multiple sclerosis, thalamic pain, Alzheimer's disease, spastic paraplegia, cerebral palsy and downs [sic] syndrome because of its ability to be inserted into the sphenoid sinus and its actions controlled" (col. 3, line 66 – col. 4, line 6); and
- "The apparatus of this invention may be useful in treating a number of diseases because of its ability to stimulate the pituitary

gland and surrounding neurological and brain structures through the sphenoid sinus" (col. 6, line 66 – col. 7, line 2).

Neither of these explanations suggests the involvement of the SPG.

Applicant thus submits that independent claim 178 is allowable over Shantha. Claims 1, 6, 10-14, 19, 23-24, 27, 30-31, 33-34, 40, 47, 179, and 182-185 directly or indirectly depend from claim 178, and thus are also in a condition for allowance, being of narrower scope than the allowable independent claim from which they depend.

The amendments to claim 178, and new dependent claim 185, find support *inter alia* on p. 49, lines 26-27 of the specification as filed, and in claims 5, 20, 48, 105, and 116 as originally filed.

#### *New claim 186*

New claim 186 recites the features of dependent claim 47 and independent claim 178 as previously presented (and is similar, though not identical to, claim 47 as originally filed). As mentioned above, dependent claim 47 was rejected under 35 U.S.C. 103(a) as being unpatentable over Shantha in view of Suzuki. The Examiner argued, "It is well-known that blood carries the oxygen and nutrients needed for proper brain function; therefore an increase of blood flow to the brain would necessarily have a salubrious effect on a patient suffering from Alzheimer's disease." Applicant respectfully traverses the rejection of dependent claim 47, and thus submit that claim 186 is allowable, as are claims 48, 187, and 188 which directly or indirectly depend from claim 186.

Applicant respectfully submits that the Examiner has improperly taken official notice regarding the relationship between blood flow, oxygen and nutrient supply, and Alzheimer's disease. "As noted by the court in *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970), the notice of facts beyond the record which may be taken by the examiner must be 'capable of such instant and unquestionable demonstration as to defy dispute'" (MPEP 2144.03). Furthermore, "It is never appropriate to rely solely on 'common knowledge' in the art without evidentiary support in the record, as the principal evidence upon which a rejection was based. *Zurko*, 258 F.3d at 1385, 59 USPQ2d at 1697" (MPEP 2144.03).

Applicant respectfully submits that it is not at all well-known or commonly believed that "an increase of blood flow to the brain would necessarily have a salubrious effect on a patient suffering from Alzheimer's disease," as asserted by the Examiner. Instead, what is indeed well-

known is that the most common theory for the pathogenesis of Alzheimer's disease is the amyloid hypothesis (see, for example, p. 4, lines 14-24 of the application as filed). The deposition of A $\beta$  in plaques has no inherent or commonly-understood relationship to oxygen or nutrient supply. Applicant thus respectfully traverses the Examiner's unsubstantiated assertion of common knowledge, and note that the "the examiner must provide documentary evidence in the next Office action if the rejection is to be maintained" (MPEP 2144.03).

Applicant further submits that although some researchers have recently considered vascular factors prominent in the pathophysiology of Alzheimer's disease (see, for example, p. 65, lines 29-30 of the application as filed), the existence of such a vascular hypothesis would not lead one of ordinary skill in the art to expect that the stimulation of SPG-related tissue would treat Alzheimer's disease. Even J.C. de la Torre, one proponent of this vascular hypothesis, acknowledges that although several experimental drug therapies for Alzheimer's disease share the effect of improving or increasing cerebral perfusion, the effectiveness of such therapies "in reducing the symptoms or delaying the progress of AD is debatable" (p. 199-200 of de la Torre JC, "Vascular Basis of Alzheimer's Pathogenesis," Ann N.Y. Acad Sci 977: 196-215 (2002), cited in the Information Disclosure Statement submitted on September 2, 2008). (Applicant notes that the de la Torre article published after the filing dates of two of the present application's priority applications, PCT Patent Application PCT/IL 01/00402, filed May 7, 2001, and U.S. Provisional Patent Application 60/203,172, filed May 8, 2000.)

#### ***Information Disclosure Statement***

The Examiner requested that Applicant point out any particular references in the Information Disclosure Statements which they believe may be of particular relevance to the instant claimed invention. Applicant is not aware of any references of greater relevance than those already of record and applied by the Examiner, and the de la Torre article discussed hereinabove.

#### ***Withdrawal of restriction requirement***


Claims 1, 6, 10-14, 19, 23-24, 27, 30-31, 33-34, and 40 were withdrawn in response to a restriction requirement. Given the suggested patentability of independent claim 178, from which these non-elected claims directly or indirectly depend, the Applicant respectfully submits

that the restriction requirement with respect to these withdrawn claims should be withdrawn (MPEP 821.04) and the claims rejoined.

Applicant believes the amendments and remarks presented hereinabove to be fully responsive to all of the grounds of rejection raised by the Examiner. In view of these amendments and remarks, Applicant respectfully submits that all of the claims in the present application are now in order for allowance. Notice to this effect is respectfully requested.

Respectfully submitted,

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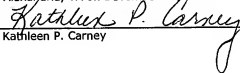
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The Director is hereby authorized to charge or credit Deposit Account No. **18-0350** for any additional fees, or any underpayment or credit for overpayment in connection herewith.

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